UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,565	08/09/2001	Preeti Lal	PF-0450-1 DIV	6831

27904 7590 01/16/2004

INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/927,565	LAL ET AL.	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *5-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8/09/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group I (claims 1-4) in Paper No: 10/22/03 is acknowledged. The traversal is on the ground(s) that "method claims 5, 8, 11-12, 15, and 18, all of which depend from and are of the same scope as product claim 1 of Group I, and could therefore be examined together with the product claims themselves without serious burden", and cites *In re Ochiai*. This is not found persuasive because the methods of Groups II, IV, VI, VII & IX require different starting materials (e.g., samples to be tested, substrates, standards, protocols, binding reactions, animals, etc.) not required in Group I, which therefore, are not equivalent in scope to the products and method in Group I. A serious burden further exists because of the different goals and method steps required for the claims of Groups II, IV, VI, VII & IX , which are not required for examination of the products of Group I, and for the reasons previously made of record in Paper No: 5 (mailed 9/25/03). Thus, the requirement is still deemed proper and is therefore made FINAL.

Claims 7-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No: 10/22/03.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 & 3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification describes on pages 4 & 6 the human preproneurotensin/neuromedin N (HPPN) polypeptide of SEQ ID NO: 1, as well as the bovine and rat polypeptide sequences. However, page 7 of the specification states that "HPPN, as used herein, refers to the amino acid sequences of substantially purified HPPN obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and preferably the human species, from any source...". However, the sole single human polypeptide species described is the HPPN polypeptide of SEQ ID NO: 1, in which none of these other species of HPPN polypeptides are described, except for the bovine sequence. In other words, no written description is provided in the specification for any different species of HPPN polypeptide molecules, nor for any "naturally occurring" allelic and/or splice variants thereof comprising at least 90% sequence identity to SEQ ID NO: 1, nor any additional generic sequences thereof that merely "***comprise***... a fragment/biologically active portion of SEQ ID NO: 1". Nor is any written description provided for what distinguishable and assayable functional characteristics any generic polypeptide would possess, since none are recited in the claims. In other words, one skilled in the art can not reasonably structurally visualized any other functional amino acid sequence, except for the single disclosed *human* sequence of SEQ ID NO: 1; thereby, not currently meeting the written description requirements of 35 U.S.C. 112, first paragraph.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999 (e.g., see Examples 11 and 13). See also MPEP 2163.

3. Claims 1 & 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while then being enabling for the specific polypeptide of SEQ ID NO: 1, does not reasonably provide enablement for any polypeptide sequence merely comprising any biologically functional equivalent fragment /antigenic epitope, or to any variant polypeptide with no recited distinguishable and assayable function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The name "naturally occurring polypeptide" or "biologically active fragment", etc. (as it relates to how it is defined on pages 14 & 15, etc. of the specification) encompasses any polypeptide with "substituted, inserted or deleted" amino acid residues, or any biological functional equivalent molecule, which sets forth little structural characterization and no functional characteristics. In contrast, the specification does not teach which particular encoded amino acids are critical for any HPPN protein's function; nor how to distinguish the claimed HPPN-related polypeptides from any other polypeptide molecule that possesses none of the desired functions of the instant invention. Therefore, any such broadly claimed polypeptides without further definable functional characteristics would be expected by the skilled artisan to result in inactive proteins. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means

have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any distinguishable and assayable HPPN function would prevent the skilled artisan from determining whether any modification or mutation or truncation to the single disclosed human HPPN molecule of the instant invention could be made which retains the desired function of the instant invention, because any random mutation or modification or truncation manifested within a HPPN protein would be predicted to adversely alter the biologically active 3-dimensional conformation of the protein, without requiring undue experimentation to determine otherwise.

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 & 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bean et al. (1991), in view of the 1989/1990 Promega Protocols and Application Guide.

Bean et al. teach a naturally occurring human neurotensin/neuromedin N protein that is 100% identical with residues 1-120 of SEQ ID NO:1 (i.e., 100% identical with a query match of 70.3%; pg. 263; Fig. 1; as it relates to claim 1b), and therefore, also "comprises... a biologically active fragment/immunogenic fragment... of SEQ ID NO:1" (i.e., as it relates to claims 1c& d). Although Bean teach cloning their HPPN molecule in a pGEM4 expression vector, Bean does not specifically teach isolation of this polypeptide.

The Promega Protocol and Application Guide teaches how to produce and isolate proteins encoded by DNA sequences inserted into a lacZ/pGEM vector following expression of the lacZ-fusion protein in the presence of IPTG prior to cell lysis (pgs. 96-98 & 188-189). In that the resultant isolated proteins are routinely stored in a pharmaceutically acceptable carrier that comprises water, TBS or TEP buffer, the limitations of claim 3 are met. However, the Promega Guide does not teach the specific purification of a HPPN polypeptide expressed from Beans' DNA.

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use methods well known in the art, such as Promega's expression and isolation/purification system, to make a composition comprising the HPPN protein expressed from Bean's constructs, because such is routine in the art, and because Bean et al teach on pages 259-260 that HPPN may be involved in the etiology of schizophrenia, and therefore, may be of clinical relevance.

5. Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dong et al. (3/1997; IDS Ref #19), in view of the 1989/1990 Promega Protocols and Application Guide.

Dong et al teach the complete DNA sequence encoding the HPPN polypeptide of SEQ ID NO: 1 (GenBank Accession No. U91618). However, Dong et al do not teach isolation and expression of their HPPN protein.

Promega is as discussed above. In addition, the Promega Guide teaches cDNA cloning into lacZ-fusion vectors (e.g., pGEM2 or pGEM4; pgs. 185-187). However, the Promega Guide does not teach the specific purification of a HPPN polypeptide expressed from Dong's DNA.

It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to use methods well known in the art, such as Promega's expression and isolation/purification system, to make a composition comprising the HPPN protein expressed from Dong's DNA molecule, because such is routine in the art, and because neurotensin and neuromedin N are important hormones well known in the art.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RCH

Robert C. Hayes, Ph.D.
January 12, 2003

pat Sig
1600